REMARKS

Status of the Claims

Claims 1, 3 to 9, 21, 22 and 25 to 27 were pending as shown in the response filed November 25, 2005. Claim 1 has been amended as suggested by the Examiner and to remove the recitation to "derivative thereof." As indicated throughout the specification as filed, an antibody refers to any antibodies or derivatives thereof described on page 15, lines 8-12. Claims 7, 21 and 25 have also been amended to clarify antecedent basis. Thus, claims 1, 3-9, 21, 22, 25, 26 and 27 are pending as shown above.

Rejections Withdrawn

Applicants note with appreciation that the rejections under 35 U.S.C. § 112, 1st and 2nd paragraphs and 35 U.S.C. § 103 over Contag in view of Georgiou have been withdrawn.

35 U.S.C. §112, 2nd Paragraph

Claims 1, 3-9, 21, 22 and 25-27 were rejected as allegedly indefinite. (Office Action, page 4). Claim 1 was alleged to be indefinite for reciting "derivative thereof." *Id.* Claims 7, 21 and 25 were alleged to have insufficient antecedent basis. *Id.*

Claim 1 has been amended to remove the term "derivative thereof," thereby obviating the rejection. Applicants note for the record that the term "antibody" is definite and clearly encompasses polyclonal antibodies, monoclonal antibodies, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')2 fragments, fragments produced by an Fab expression library, anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of these antibodies. *See,* page 15, lines 8-12 of the specification.

Claims 7, 21 and 25 have also been amended as shown above to provide clear antecedent basis. Thus, the rejections have been obviated and withdrawal thereof is respectfully requested.

35 U.S.C. §103

Claims 1, 3-9, 22-23 and 27 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,521,066 (hereinafter "Menzel") in view of U.S. Patent No. 5,348,867 (hereinafter "Georgiou"). (Office Action, pages 5-6).

Menzel was cited for disclosing a transmembrane fusion protein comprising a ligand binding domain, a cytoplasmic toxR NDA binding region, a hydrophobic ToxR transmembrane region and a reporter gene operably linked to the ctx operon. *Id.* Menzel was further alleged to disclose that binding a ligand to the ligand binding domain induces a conformational change in the cytoplasmic domain, which in turn induces binding to the promoter region of the reporter gene. *Id.* While the Office Action states that Menzel does not explicitly disclose use of antibodies on the bacterial surfaces, it was alleged that it would have been obvious to use Georgiou's heterologous scFV antibodies in Menzel's fusion proteins. *Id.*

Because Menzel, alone or in combination with Georgiou fails to teach the claimed biodetectors, Applicants traverse the rejection and supporting remarks.

The pending claims are drawn to biodetectors comprising 3 elements: (1) a transmembrane fusion protein having an extracellular antibody domain and an intracellular domain which is activated upon binding of a selected substance to the antibody; (2) a transducer which is activated by the activated intracellular domain of the transmembrane fusion protein; and (3) a transcription activation element that is activated by said active form of the transducer, to give a detectable signal.

As admitted by the Office, Menzel fails to teach a fusion protein having an extracellular antibody domain. Instead, Menzel's system is based on the dimerization. *See, e.g.,* Abstract and claim 1 of Menzel. The ligand binding domain is optional and expression of the reporter gene is linked to dimer formation, not ligand binding (see, Menzel, Abstract, col. 1, line 65 to col. 2, line 6, emphasis added):

> The present invention relates to:
> (1) a fusion protein having a dimerizing domain **with or without a ligand-binding region** and toxR DNA-binding and hydrophobic transmembrane regions;....

> The present invention relates to host cells comprising (a) a transmembrane fusion protein having (i) a periplasmic dimerization domain (e.g., a ligand-binding domain) and (ii) a toxR region having a cytoplasmic toxR DNA-binding region and a hydrophobic toxR transmembrane region, and (b) a nucleic acid molecule having a reporter gene operatively linked to the ctx operon, wherein dimer formation, **which may or may not involve ligand binding**, is signaled by expression of the reporter gene.

Thus, Menzel does not teach or suggest a biodetector in which the extracellular domain is an antibody which binds to a ligand and in which binding of the ligand triggers (via a cascade) expression of the reporter gene, as claimed.

Furthermore, because Menzel's system is based on dimerization, there is no motivation to substitute Georgiou's scFV antibodies for Menzel's dimerization domain or ligand binding domain. In fact, because such substitutions would destroy the intended function of Menzel's system, the 103 rejection cannot stand.

In addition, Menzel also fails to teach or suggest a transducer that is activated by the intracellular domain as claimed. Rather, Menzel teaches that the intracellular DNA-binding domain itself "has the capacity to activate expression from the ctx operon." *See,* col. 2, lines 12-15 of Menzel. In other words, there is no "transducer" is Menzel's system -- the intracellular portion of the fusion protein itself activates expression of the reporter gene (via the ctx operon).

In sum, Menzel does **not** disclose or suggest a transmembrane fusion protein whose intracellular portion is activated by binding to the extracellular antibody portion; a transducer which is activated by the activated intracellular portion of the fusion protein; and/or a responsive element that is activated by the activated from of the transducer.

Georgiou does not cure the deficiencies of Menzel. Indeed, combining Georgiou's disclosure of expressing proteins (including scFV fragments) on the surface of cells with Menzel's dimerization detecting systems cannot result in the claimed biodetectors.

Thus, the Office has not established that the fusion proteins described in Menzel are biodetectors as set forth in the pending claims or that the combination of Menzel and Georgiou can in any way result in biodetectors as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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By: _____
Dahna Pasternak
Registration No. 41,411
Attorney for Applicants

ROBINS & PASTERNAK LLP
1731 Embarcadero Road, Suite 230
Palo Alto, CA 94303
Telephone (650) 493-3400
Facsimile (650) 493-3440